

Ciliary neurotrophic factor in the hypothalamus of obese mice

Antonio Giordano, Ilenia Severi and Jessica Perugini

Department of Experimental and Clinical Medicine, School of Medicine, Università Politecnica delle Marche, Ancona, Italy.

Ciliary neurotrophic factor (CNTF) is a potent survival molecule for a large number of neuronal and glial cells. We previously found that in mouse hypothalamus CNTF is expressed by ependymal cells and tanycytes lining the third ventricle and in a few scattered glial cells (Severi et al., 2012). Exogenously administered CNTF produces an anorectic effect via activation of hypothalamic neurons, and also stimulates neurogenesis in mouse hypothalamus. Thus, we evaluated CNTF expression in the hypothalamus of mice feeding a high fat diet (HFD, 50% of calories as fat) and in mice kept in a calorie restriction (CR) regimen (60% of individual mean food intake). RT-PCR showed a significant increase of both CNTF and CNTF receptor α (CNTFR α) mRNAs in the hypothalamus of the HFD mice; conversely, CR mice exhibited a significant decrease of CNTF and CNTFR α . Immunohistochemistry showed that in the HFD mice the hypothalamic increase of CNTF was restricted to the tanycytes located in the ependymal layer bordering the median eminence and sending their processes to the arcuate, ventromedial and dorsomedial nuclei, the tuberal part of the hypothalamus strongly involved in energy balance regulation. Stimulation of cells bearing the CNTFR α induces specific activation of the signal transducer and activator of transcription 3 (STAT3) signalling system. Intraperitoneal treatment with recombinant CNTF and detection of the nuclear expression of phospho-STAT3 (P-STAT3) confirmed an increased responsiveness of HFD mice hypothalamus to CNTF and, conversely, a decreased expression of the receptor in the mice kept in the CR regimen. Interestingly, only in the HFD mice CNTF was able to activate a large population of neurons dispersed in the arcuate, ventromedial and dorsomedial nuclei. These data suggest that hypothalamic CNTF is a new central modulator of energy balance neuronal networks, possibly involved in the increased neurogenesis seen in the hypothalamus of obese mice.

References

- [1] Severi et al. (2012) Constitutive expression of ciliary neurotrophic factor in mouse hypothalamus. *J Anat* 220: 622-631.

Key words

Obesity, calorie restriction, tanycytes, neuropeptides, growth factors.